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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/576,715	05/23/00	HATAKEYAMA	K 2000 0644A

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EXAMINER	
FORMAN, B	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/576,715	HATAKEYAMA, KAZUHISA	
	Examiner	Art Unit	
	BJ Forman	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 May 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-12 are indefinite in Claim 1 because the claims are drawn to a method for gene analysis but the claim does not recite method steps of gene analysis. Method claims need not recite all operating details but should at least recite positive, active steps so that the claims will set out and circumscribe a particular area with a reasonable degree of precision and particularity and make clear what subject matter that claims encompass as well as make clear the subject matter from which others would be precluded. *Ex parte Erlich*, 3 USPQ2d 1011 at 6. It is suggested that Claim 1 be amended to recite positive active method steps for gene analysis as described in the specification e.g. hybridizing, immobilizing, detecting, binding, quantifying, comparing, analyzing.

b. Claims 1-12 are indefinite in Claim 1 for the recitation "the hybridization is caused in the presence of a double-stranded DNA-binding protein." because "caused" is a non-specific activity and therefore it is unclear how the hybridization is "caused" by the presence of the protein. It is suggested that Claim 1 be amended to clarify i.e. replace "caused" with "stabilized" (specification, page 6, line 20-22).

c. Claim 10 is indefinite in the recitation "intensity of hybridization signal" because "intensity" and "signal" lack proper antecedent basis in Claim 1 which does not recite a label having an "intensity" and/or "signal". It is suggested that Claim 10 be amended to provide

proper antecedent basis e.g. amend the claim to depend from Claim 9 and replace "hybridization signal" with "signal from the labeled hybridization".

d. Claim 11 is indefinite in the recitation "then polymorphism in the target sequence is detected based on the result of detection of hybridization" because the recitation is incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the elements for detecting a polymorphism based on the hybridization signal. It is suggested that the claim be amended to recite the missing elements as described in the specification e.g. labeled nucleic acids, signal intensity, comparison of signal intensity to control.

e. Claim 12 is indefinite in the recitation "then nucleotide sequence of the sample nucleic acid is determined based on the result of detection of hybridization" because the recitation is incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the elements for determining nucleotide sequence based on the hybridization signal. It is suggested that the claim be amended to recite the missing elements as described in the specification e.g. labeled nucleic acids, signal intensity, comparison of signal intensity to control.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-2 & 11-13 rejected under 35 U.S.C. 102(b) as being clearly anticipated by Wagner et al. (WO 93/02216, published 4 February 1993).

Regarding Claim 1, Wagner et al. disclose a method for gene analysis comprising the step of detecting hybridization between a probe nucleic acid and a sample nucleic acid containing a target sequence that has sequence complementary to that of the probe nucleic acid, wherein the probe nucleic acid is immobilized on a substrate, at least one of the probe nucleic acid and the sample nucleic acid is DNA and the hybridization is caused in the presence of a double-stranded DNA-binding protein (page 6, lines 1-28). The hybridization being caused in the presence of a double-stranded DNA-binding protein is interpreted by the examiner as hybridization "occurs" in the presence of a double-stranded DNA-binding protein because nucleic acids having complementary sequences, as recited in Claim 1, are known to hybridize absent double-stranded DNA-binding proteins and therefore it is unclear how the protein "causes" hybridization which is known to occur absent the proteins.

Regarding Claim 2, Wagner et al. disclose the method wherein the sample nucleic acid is DNA (page 6, lines 25-28).

Regarding Claim 11, Wagner et al. disclose the method wherein detecting hybridization is performed using a plurality of probe nucleic acids and a polymorphism in the target sequence is detected based on the detection of hybridization (Example 1, page 40, lines 19-26 and Fig. 1).

Regarding Claim 12, Wagner et al. disclose the method wherein detecting hybridization is performed using a plurality of probe nucleic acids and nucleotide sequence of the target sequence is determined based on the detection of hybridization i.e. the detection of hybridization determines whether the target is wild-type or mutant sequence (Example 1, page 40, lines 19-26 and Fig. 1).

Regarding Claim 13, Wagner et al. disclose a test kit for detection of hybridization between a probe nucleic acid and a sample nucleic acid containing a target sequence that has a sequence complementary to that of the probe nucleic acid, said kit comprises at least a double-stranded DNA-binding protein (page 9, lines 3-20).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 3-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wagner et al. (WO 93/02216, published 4 February 1993) in view of Guagliardi et al. (Journal of Molecular Biology, 1997, 267: 841-848) and SwisProt (accession No. 059631, 15 December 1998 and accession No. P39476; P81550, 1 February 1995).

Regarding Claims 3-8, Wagner et al. teach the method for gene analysis comprising the step of detecting hybridization between a probe nucleic acid and a sample nucleic acid containing a target sequence that has sequence complementary to that of the probe nucleic acid, wherein the probe nucleic acid is immobilized on a substrate, at least one of the probe nucleic acid and the sample nucleic acid is DNA and the hybridization occurs in the presence of a double-stranded DNA-binding protein (page 6, lines 1-28) but they do not teach the double-stranded DNA-binding protein is derived from a hyperthermophilic bacterium. Guagliardi et al. teach a similar method for gene analysis comprising detecting hybridization between nucleic acids wherein the nucleic acids are DNA and the hybridization occurs in the presence of a double-stranded DNA-binding protein wherein the protein is Sso7d (page 843, right column, third full paragraph) which is derived from a hyperthermophilic bacterium (Claim 3), derived from an archaebacterium (Claim 4), derived from a bacterium belonging to the genus *Sulfolubus* (Claim 5), derived from *Sulfolubus solfataricus* (Claim 6) and is the Sso7d protein derived from *Sulfolubus solfataricus* (Claim 7) as taught by Guagliardi et al. (page 841, right column, first full paragraph). Additionally, Guagliardi teach the sequence of the Sso7d is

known (page 841, right column, lines 9-18) and SwissProt specifically teaches the sequence accession No. 059631; P39476; and P81550) (Claim 8). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the DNA-binding protein in the method of Wagner et al. with the Sso7d protein taught by Guagliardi et al. having the known amino acid sequence, for the expected benefit of analyzing genes with reduced time of hybridization, at higher temperatures and with increased specificity as taught by Guagliardi et al. (page 847, right column, lines 3-6).

Regarding Claim 9, Wagner et al. do not teach the method comprising labeled sample nucleic acids. Guagliardi et al. teach the similar method wherein the sample nucleic acids are labeled wherein the label facilitates identification and comparison of nucleic acids bound and unbound to the DNA-binding protein by permitting simple visual inspection of a polyacrylamide gel (page 844, Fig. 2a, page 845, Fig. 3b and page 846, Fig 5).

Regarding Claim 10, Wagner et al. do not teach the method wherein the amount of the sample nucleic acid containing the target sequence is analyzed. Guagliardi et al. teach the similar method wherein the amount of target sequence is analyzed i.e. the intensity of the labeled nucleic acids bound and unbound to the DNA-binding proteins is analyzed to determine the amount of nucleic acids bound (% annealed product) (page 844, Fig. 2b and page 845, Fig. 3a & Fig. 4a).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify sample nucleic acids of Wagner et al. by labeling the sample nucleic acids as taught by Guagliardi et al. for the expected benefit of simplifying nucleic acid sequence analysis by merely visualizing a polyacrylamide gel to thereby identify and compare sequences bound and unbound to the DNA-binding protein as illustrated in the figures of Guagliardi et al. It would have been further obvious to one skilled in the art to label the sample nucleic acids with a quantifiable label for the expected benefit of quantifying the gene analysis in the method of Wagner et al. by merely quantifying the label.

Conclusion

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:45 TO 4:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
January 5, 2001

W. Gary Jones
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1/10/01